

## **REMARKS**

### **Claim rejections – 35 USC 103**

In view of the preceding amendments and of Applicants showing of the obtention of unexpected effects as set forth in the last amendment filed on 22 February 2010, the Office has now issued a new rejection of claims 12-21 and 25-26 under 35 USC 103(a) as being unpatentable over Johnson WO99/18065 in view of Zhang et al., J Org Chem, 1999, 64(6), pp. 1774-75.

Under item (5) of the office action, the Examiner acknowledges that Johnson fails to teach Applicant's particular hydrogenation catalyst metal. The Examiner relies on Table 1 of Zhang, which discloses a Rh-catalyzed asymmetric hydrogenation of an enamide in a purportedly analogous process.

The office action states on page 3, second paragraph, that the catalyst used by Johnson is "a complex of a transition metal  $M^{2+}$  with a chiral phosphine ligand". As emphasized at the Interview on October 14, 2009, Applicants respectfully submit that Johnson teaches the use of a complex of a transition metal  $M^{2+}$  with a chiral ligand exclusively for the hydrogenation of eneamides, not for the formation of eneamides. See Johnson, reaction scheme of page 4; page 5, line 24 to page 6, line 24; and step C of Examples 1 to 7.

The claimed process for the formation of eneamide intermediates requires a specific hydrogenation step (i), namely: a hydrogenation/isomerization of an oxime of formula (II) with an acyl derivative of formula (III) in the presence of a specific heterogenous catalyst based on at least one metal selected from Ir and Rh. These eneamides intermediates are then useful for the obtention of asymmetric amines or amides by an optional second hydrogenation step (ii).

These hydrogenation steps (i) and (ii) are so specific that they cannot be done by the same hydrogenation catalyst. Accordingly those skilled in this catalyst art have developed different catalyst systems for hydrogenation steps (i) and (ii). Johnson, for example, teaches the critical use of iron in hydrogenation/isomerization step (i). See Johnson, Page 5, lines 9-23 and "step B" in Examples 1-7. Then, Johnson teaches the use of a chiral catalyst in hydrogenation step (ii), said chiral catalyst being a catalyst system derived from the complex of a transition metal  $M^2$  with a chiral phosphine ligand. See Johnson, page 5, lines 24-29. Johnson cites preferred examples of  $M^2$ , namely Rh, Ru or Ir (page 6, lines 12-13) and then complexes of Rh

with chiral ligands as disclosed in US-A-5171892 (Johnson, page 6, lines 14-24). By emphasizing the use of iron in hydrogenation/isomerization step (i) and the use of Rh, Ru or Ir, further in the form of complexes with chiral ligands, only in step (ii), Johnson teaches away from using Rh, Ru or Ir in hydrogenation/isomerization step (i).

In view of this, the first difference identified in the office action between the invention and Johnson would be more accurately stated as follows:

- (i) “Johnson et al fail to teach applicant’s particular hydrogenation catalyst metal **for the hydrogenation/isomerization step of an oxime into an eneamide.**”

Zhang adds nothing new to the Johnson disclosure. As with Johnson, Zhang describes the use of Rh phosphine ligands (see Table I) to hydrogenate the eneamide, which is hydrogenation step (ii), just as described in Johnson. Thus, for the same reasons that Johnson does not anticipate the claimed invention, Johnson in view of Zhang does not render obvious the claimed invention.

Moreover, it is respectfully submitted that limiting the list of metals for the formation of eneamide from oxime to the two exemplified metals Iridium (Ir) and Rhodium (Rh) in Examples 1 to 5 renders the claims commensurate in scope with the unexpected results shown in the Examples.

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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